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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,341	TANAKA ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) *9 and 14-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *10 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Election of Group I, claims 1-13 was made **without** traverse in the reply filed on 7 April 2005. Proteins were elected as the species of matrix complex from claim 7; gelatin was elected as the species of protein from claim 8. Claim 9 becomes drawn to an unelected species and is withdrawn from consideration.

Claims 1-8 and 10-13 are being examined for patentability; claims 9 and 14-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-64 are pending in the current application. Claims 27 and 51 have been amended. Because the election was made without traverse, the restriction requirement is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 11 is directed to the cell culture/transfection device of claim 10, wherein the surface is selected from a continuous surface, flasks, dishes, tubes, multi-well plates, slides, and implanted devices. It is not clear what a continuous surface is. It appears a continuous surface would be never ending (infinitely continuous); however, as this is not possible, it is being interpreted to mean any surface with area (i.e. a flask, a dish, a multi-well plate, a slide).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Shastri et al (US 2005/0079159 A1).

Shastri et al teach a polymer matrix for the ex vivo culture of eukaryotic cells, the matrix is intended for implantation (thus, it is applicant calls an implantation device). The matrix is to be coated with a gel matrix of gelatin to enhance cell attachment to the polymer; appropriate nutrients, including calcium chloride can also be applied to the matrix (See Pg. 6, paragraphs 0087-0088) (Claims 10 and 11). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sabatini et al (US 2002/0006664 A), in view of Qiagen ("Effectene Transfection Reagent" Product Information), further in view of Ausubel et al (Current Protocols in Molecular Biology, 1988).

Sabatini et al teach a cell culture/transfection device for transfecting eukaryotic cells, comprising a slide (which applicant calls a solid surface), spotted with DNA in a gelatin matrix (which applicant calls a gel matrix, wherein the gelatin acts as the carrier protein) (See Sabatini et al, Pg. 19, paragraphs 0187-0203).

Sabatini et al use the cell culture/transfection device to transfect eukaryotic cells in a reverse transfection method, comprising a) adding to the gelatin-DNA spots the transfection reagents (Effectene Transfection Kit, Qiagen, cat #301425, comprised of DNA-condensation buffer (EC buffer), "Enhancer," and "Effectene Transfection Reagent"), b) incubating the spots + transfection reagents, c) vacuuming off reagents, d) plating cells on top of array for reverse transfection, and e) allowing transfection to proceed for approximately 40 hours.

The ingredients of the Effectene Transfection Kit (Qiagen, cat #301425) are not specifically defined; however, based on the Current Protocols in Molecular Biology, it appears the "DNA precipitation buffer/EC buffer," is HEPES-buffered saline, the "Enhancer" is ethanol, and the "Effectene Transfection Reagent" is calcium chloride (See Ausubel et al, Pg. 9.1.1), as these are the normal reagents used, correlating to the procedural steps described by Qiagen, for calcium phosphate transfection. However, even if the "DNA precipitation buffer/EC buffer," "Enhancer" and/or "Effectene Transfection Reagent" provided by Qiagen are not HEPES-buffered saline, ethanol, and calcium chloride, respectively, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use HEPES-buffered saline, ethanol, and calcium chloride in the calcium phosphate transfection described by Sabatini et al. One of ordinary skill in the art would have been motivated to mix ethanol, calcium chloride and HEPES-buffered saline and to add the solution to the gelatin-DNA spots in order to form the calcium phosphate precipitate needed for proper transfection, as one of ordinary skill in the art knows the ethanol functions to condense the DNA, the calcium chloride forms a $CaCl_2$/DNA complex that precipitates $CaPO_4$-DNA in the HEPES-buffered saline (See Ausubel et al). One would have expected

success using HEPES-buffered saline, ethanol, and calcium chloride in place of the "Effectene Transfection Reagent Kit" because HEPES-buffered saline, ethanol, and calcium chloride are the standard protocol, known in the art, for producing calcium phosphate-DNA precipitate (See, e.g. Ausubel et al).

The reverse transfection method of Sabatini et al requires the formation of the calcium phosphate-DNA precipitate on the slide prior to administration of the cells. The calcium phosphate-DNA precipitate is formed directly on the slide by combining all of the reagents (DNA, DNA condensation buffer/EC buffer (or HEPES-buffered saline), Enhancer (or ethanol), and Effectene Transfection Reagent (or calcium chloride)) together on the slide and incubating.

The preformed gelatin-DNA slide of Sabatini et al allow for the pre-application of one of the reagents, the DNA, directly on the slide in a gelatin matrix, thus deleting the step of separately obtaining and adding the DNA. However, though Sabatini et al pre-apply the DNA onto the slides, it would have been obvious to one of ordinary skill in the art at the time the invention was made to pre-apply any of the reagents to the slide in the gelatin matrix, in order to delete the step of separately obtaining and adding any of the reagents.

Because all the reagents not pre-applied to the slide are combined in a single application to the reagent pre-applied to the slide, changing the reagent pre-applied to the slide would be considered a changing the sequence of adding the ingredients, wherein the pre-applied agent considered being added first, the non-pre-applied agents considered being added second. Because the all reagents together are necessary for the formation of the calcium phosphate-DNA precipitate, selection of any order of mixing the reagents (selection of any reagent to be pre-applied/added first) is prima facie obvious. See *In re Gibson, 39 F.2d 975, 5USPQ 230 (CCPA 1930)* and *In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946)*. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to pre-apply the calcium chloride in a gelatin matrix to the slide, to produce a cell culture/transfection device for reverse transfection of eukaryotic cells, comprising a slide coated with

calcium chloride in a gelatin matrix (Claims 10, 11 and 13). One of ordinary skill in the art would have been motivated to pre-apply the calcium chloride in a gelatin matrix instead of the DNA because the calcium chloride is not at risk of mutation or breakage; additionally, slides prepared with calcium chloride in a gelatin matrix, as opposed to DNA in a gelatin matrix, allow the user to choose which genes are being transfected, thereby customizing each array for their individual experiment.

Though the example provided Sabatini et al (Pg. 19) uses a slide to produce the array, they also teach that the arrays can be produced on the bottom of a microtitre dish (which applicant calls dishes), a culture dish, a culture chamber, tubes and any other suitable substrate geometry. Therefore, though Sabatini et al do not specifically state continuous surfaces, flasks, multi-well plates or implanted devices, it would have been obvious to one of ordinary skill in the art at the time the invention was made to create an array, including an array comprised of calcium chloride in a gelatin matrix, on any solid surface, including continuous surfaces, flasks, multi-well plates and/or implanted devices (See Sabatini et al, Pg. 11, paragraph 0104) (Claims 1-8, 11 and 13). One of ordinary skill in the art would have been motivated to use any solid surface, including continuous surfaces, flasks, dishes, tubes, multi-well plates, slides, and/or implanted devices based on their particular criteria and use of the array. One of ordinary skill in the art would be motivated to flasks, such as culture flasks, or multi-well plates, both of which are considered continuous surfaces, because they can easily hold cell culture solution; multi-well plates would especially be useful when multiple samples of different cells are to be transfected, in order to provide separate wells for each cell type. One of ordinary skill in the art would have been motivated to use an implantable device in order to transfect cells prior to transplanting them to a patient, for example, an artificial dermis matrix that is to be used to transfect cells with growth factors to increase the survive rate of the transplanted cells. One would have expected success using any geometric surface because Sabatini et al teach that any solid geometric surface, suitable for the individual needs is acceptable.

Finally, though the example provided by Sabatini et al (Pg. 19) uses a poly-L-lysine slide, they also teach that any suitable surface material can be used to produce the arrays, including glass and plastics, such as polystyrene (See Sabatini et al, Pg. 11, paragraph 0104) (Claim 12). Additionally, though they do not specifically list epoxy resins as a material, it would have been obvious to one of ordinary skill in the art to use epoxy resins as at least part of the solid surface (Claim 12). One of ordinary skill in the art would have been motivated to use cured epoxy resin plastics based on availability of materials, for example, if epoxy resin slides or dishes, or glass-reinforced plastics, that comprise epoxy, were readily available. One would have had a reasonable expectation of success using any glass, plastic, or epoxy resin material that is suitable grade for cell culture based on Sabatini et al teaching that any suitable solid material can be used.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER